

What is claimed is:

1. A method of determining the amount of 14-hydroxycodeinone contained in an oxycodone preparation comprising:
 - (a) preparing for analysis by a detection system a standard solution comprising 14-hydroxycodeinone in a known concentration;
 - (b) preparing for analysis by the detection system a sample solution comprising oxycodone from the oxycodone preparation;
 - (c) analyzing the standard solution using the detection system to obtain a measurable quantification of 14-hydroxycodeinone in the known concentration;
 - (d) analyzing the sample solution of step (b) using the detection system to obtain a measurable quantification of 14-hydroxycodeinone in the sample solution; and
 - (e) determining the amount of 14-hydroxycodeinone in the oxycodone preparation based on a comparison of the quantifications obtained for the standard solution with the quantification obtained for the sample solution.
2. A method of determining the amount of 14-hydroxycodeinone contained in an oxycodone preparation comprising:
 - (a) preparing for analysis by a detection system a standard solution comprising 14-hydroxycodeinone in a known concentration;
 - (b) preparing for analysis by the detection system a sample solution of oxycodone from the oxycodone preparation, wherein the concentration of oxycodone in the sample solution is from about 10 mg/mL to the solubility limit of the oxycodone;
 - (c) analyzing the standard solution using the detection system to obtain a measurable quantification of 14-hydroxycodeinone in the known concentration;
 - (d) analyzing the sample solution of step (b) using the detection system to obtain a measurable quantification of 14-hydroxycodeinone in the sample solution; and
 - (g) determining the amount of 14-hydroxycodeinone in the oxycodone preparation based on a comparison of the quantifications obtained for the standard solution with the quantification obtained for the sample solution.
3. The method of claim 1, wherein the detection system is an HPLC system and the quantification is a measurable peak area.
4. The method of claim 2, wherein the detection system is an HPLC system and the quantification is a measurable peak area.

5. The method of claim 1 or 2, wherein the concentration of the standard solution is about 10 ppm.
6. The method of claim 1 or 2, wherein the concentration of oxycodone in the sample solution is about 50 mg/mL.
7. The method of claim 3 or 4, wherein the standard solution, the sample solution, or both are adjusted to a pH of about 7.0 to about 11.0.
8. The method of claim 3 or 4, wherein the HPLC system of the present invention has a column maintained at a temperature of from ambient temperature to about 60 degrees C, preferably at about 40 degrees C, to obtain a measurable peak area of 14-hydroxycodeinone.
9. The method of claim 1 or 2, which can provide for the detection of 14-hydroxycodeinone from about 5 ppm to about 100 ppm.
10. The method of claim 1 or 2, which can provide for the detection of 14-hydroxycodeinone from about 5 ppm to about 50 ppm.
11. The method of claim 1 or 2, which can provide for the detection of 14-hydroxycodeinone from about 5 ppm to about 25 ppm.
12. The method of claim 1 or 2, which can provide for the detection of 14-hydroxycodeinone from about 5 ppm to about 10 ppm.
13. The method of claim 1 or 2, which can provide for the detection of 14-hydroxycodeinone at about 5 ppm.
14. The method of claim 1 or 2, which can provide for the detection of 14-hydroxycodeinone at an amount less than about 5 ppm.
15. The method of claim 3 or 4, wherein the HPLC system comprises a mobile phase adjusted to a pH of about 7.0 to about 11.0, or about 7.0 to about 8.0.
16. The method of claim 15, wherein the mobile phase is adjusted to a pH of about 7.8.

17. The method of claim 3 or 4, wherein the HPLC system is selected from the group consisting of an adsorption chromatography system, an ion-exchange chromatography system and a size exclusion chromatography system.
18. The method of claim 17, wherein the HPLC system is an adsorption chromatography system.
19. The method of claim 18, wherein the adsorption chromatography system is selected from the group consisting of a normal phase chromatography system and a reverse phase chromatography system.
20. The method of claim 19, wherein the adsorption chromatography system is a reverse phase chromatography system.
21. The method of claim 3 or 4, wherein the HPLC system comprises a column maintained at a temperature from ambient temperature to about 60 degrees C.
22. The method of claim 21, wherein the column is maintained at a temperature of about 40 degrees C to about 60 degrees C.
23. The method of claim 3 or 4, wherein the HPLC system further comprises a mobile phase.
24. The method of claim 23, wherein the mobile phase comprises methanol.
25. The method of claim 23, wherein the mobile phase comprises acetonitrile.
26. The method of claim 23, wherein the mobile phase comprises phosphate buffer.
27. The method of claim 23, wherein the mobile phase comprises methanol, water, phosphate buffer and sodium dodecyl sulfate.
28. The method of claim 23, wherein the delivery of the mobile phase is from about 0.1 to about 2.0 mL per minute.

29. The method of claim 28, wherein the delivery of the mobile phase is about 0.7 mL per minute.
30. The method of claim 3 or 4, wherein the HPLC system comprises a detector selected from the group consisting of a refractive index detector, an ultraviolet detector, a fluorescent detector, a radiochemical detector, an electrochemical detector, a near-infra red detector, a mass spectrometry detector, a nuclear magnetic resonance detector and a light scattering detector.
31. The method of claim 31, wherein the detector is an ultraviolet detector.
32. The method of claim 31, wherein the ultraviolet detector is selected from the group consisting of a fixed wavelength detector, a variable wavelength detector and a diode array detector.
33. The method of claim 32, wherein the ultraviolet detector is a fixed wavelength detector.
34. The method of claim 33, wherein the fixed wavelength detector measures at a wavelength of from about 200 nm to about 275 nm.
35. The method of claim 34, wherein the fixed wavelength detector measures at a wavelength of about 220 nm.
36. The method of claim 1 or 2, wherein the concentration of 14-hydroxycodeinone in the standard solution is in an amount of from about 1 ppm to about 500 ppm of solvent.
37. The method of claim 36, wherein the concentration of 14-hydroxycodeinone in the standard solution is in an amount of from about 1 ppm to about 20 ppm of solvent or 10 ppm of solvent.
38. The method of claim 37, wherein the concentration of oxycodone in the sample solution is about 50 mg/mL.
39. The method of claim 3 or 4, wherein the HPLC system comprises an autoinjector with an injection volume of from about 1 microliters to about 100 microliters.
40. The method of claim 45, wherein the injection volume is from about 1 microliters to about 10 microliters.

41. The method of claim 46, wherein the injection volume is about 5 microliters.
42. The method of claim 3 or 4, wherein the HPLC system utilizes isocratic elution.
43. The method of claim 3 or 4, wherein the HPLC system utilizes gradient elution.
44. The method of claim 23, wherein the mobile phase comprises from about 50% aqueous medium to about 85% aqueous medium.
45. The method of claim 23, wherein the mobile phase comprises from about 60% aqueous medium to about 75% aqueous medium.
46. The method of claim 23, wherein the mobile phase comprises from about 50% methanol to about 15% methanol.
47. The method of claim 23, wherein the mobile phase comprises from about 40% methanol to about 25% methanol.
48. The method of claim 23, wherein the mobile phase comprises about 50% aqueous medium and about 50% methanol.
49. The method of claim 23, wherein the mobile phase comprises about 60% aqueous medium and about 40% methanol; or about 75% aqueous medium and about 25% methanol.
50. The method of claims 1 or 2, wherein the oxycodone preparation is oxycodone hydrochloride active pharmaceutical ingredient.
51. A method of determining the amount of codeinone contained in an oxycodone preparation comprising:
 - (a) preparing for analysis by a detection system a standard solution comprising codeinone in a known concentration;
 - (b) preparing for analysis by the detection system a sample solution comprising oxycodone from the oxycodone preparation;
 - (c) analyzing the standard solution using the detection system to obtain a measurable quantification of codeinone in the known concentration;

(d) analyzing the sample solution of step (b) using the detection system to obtain a measurable quantification of codeinone in the sample solution; and

(e) determining the amount of codeinone in the oxycodone preparation based on a comparison of the quantifications obtained for the standard solution with the quantification obtained for the sample solution.

52. A method of determining the amount of codeinone contained in an oxycodone preparation comprising:

(a) preparing for analysis by a detection system a standard solution comprising codeinone in a known concentration;

(b) preparing for analysis by the detection system a sample solution of oxycodone from the oxycodone preparation, wherein the concentration of oxycodone in the sample solution is from about 10 mg/mL to the solubility limit of the oxycodone;

(c) analyzing the standard solution using the detection system to obtain a measurable quantification of codeinone in the known concentration;

(d) analyzing the sample solution of step (b) using the detection system to obtain a measurable quantification of codeinone in the sample solution; and

(g) determining the amount of codeinone in the oxycodone preparation based on a comparison of the quantifications obtained for the standard solution with the quantification obtained for the sample solution.

53. The method of claim 51, wherein the detection system is an HPLC system and the quantification is a measurable peak area.

54. The method of claim 52, wherein the detection system is an HPLC system and the quantification is a measurable peak area.

55. The method of claim 51 or 52, wherein the concentration of the standard solution is about 10 ppm.

56. The method of claim 51 or 52, wherein the concentration of oxycodone in the sample solution is about 50 mg/mL.

57. The method of claim 53 or 54, wherein the standard solution, the sample solution, or both are adjusted to a pH of about 7.0 to about 11.0.

58. The method of claim 53 or 54, wherein the HPLC system of the present invention has a column maintained at a temperature of from ambient temperature to about 60 degrees C, preferably at about 40 degrees C, to obtain a measurable peak area of codeinone.

59. The method of claim 51 or 52, which can provide for the detection of 14-hydroxycodeinone from about 5 ppm to 100 ppm.

60. The method of claim 51 or 52, which can provide for the detection of 14-hydroxycodeinone from about 5 ppm to about 50 ppm.

61. The method of claim 51 or 52, which can provide for the detection of 14-hydroxycodeinone from about 5 ppm to about 25 ppm.

62. The method of claim 51 or 52, which can provide for the detection of 14-hydroxycodeinone from about 5 ppm to about 10 ppm.

63. The method of claim 51 or 52, which can provide for the detection of 14-hydroxycodeinone at about 5 ppm.

64. The method of claim 51 or 52, which can provide for the detection of 14-hydroxycodeinone in an amount less than about 5 ppm.

65. The method of claim 53 or 54, wherein the HPLC system comprises a mobile phase adjusted to a pH of about 7.0 to about 11.0, or about 7.0 to about 8.0.

66. The method of claim 65, wherein the mobile phase is adjusted to a pH of about 7.8.

67. The method of claim 53 or 54, wherein the HPLC system is selected from the group consisting of an adsorption chromatography system, an ion-exchange chromatography system and a size exclusion chromatography system.

68. The method of claim 67, wherein the HPLC system is an adsorption chromatography system.

69. The method of claim 68, wherein the adsorption chromatography system is selected from the group consisting of a normal phase chromatography system and a reverse phase chromatography system.

70. The method of claim 69, wherein the adsorption chromatography system is a reverse phase chromatography system.

71. The method of claim 53 or 54, wherein the HPLC system comprises a column maintained at a temperature from ambient temperature to about 60 degrees C.

72. The method of claim 71, wherein the column is maintained at a temperature of about 40 degrees C to about 60 degrees C.

73. The method of claim 53 or 54, wherein the HPLC system further comprises a mobile phase.

74. The method of claim 73, wherein the mobile phase comprises methanol.

75. The method of claim 73, wherein the mobile phase comprises acetonitrile.

76. The method of claim 73, wherein the mobile phase comprises phosphate buffer.

77. The method of claim 73, wherein the mobile phase comprises methanol, water, phosphate buffer and sodium dodecyl sulfate.

78. The method of claim 73, wherein the delivery of the mobile phase is from about 0.1 to about 2.0 mL per minute.

79. The method of claim 78, wherein the delivery of the mobile phase is about 0.7 mL per minute.

80. The method of claim 53 or 54, wherein the HPLC system comprises a detector selected from the group consisting of a refractive index detector, an ultraviolet detector, a fluorescent detector, a radiochemical detector, an electrochemical detector, a near-infra red detector, a mass spectrometry detector, a nuclear magnetic resonance detector and a light scattering detector.

81. The method of claim 81, wherein the detector is an ultraviolet detector.

82. The method of claim 81, wherein the ultraviolet detector is selected from the group consisting of a fixed wavelength detector, a variable wavelength detector and a diode array detector.
83. The method of claim 82, wherein the ultraviolet detector is a fixed wavelength detector.
84. The method of claim 83, wherein the fixed wavelength detector measures at a wavelength of from about 200 nm to about 275 nm.
85. The method of claim 84, wherein the fixed wavelength detector measures at a wavelength of about 220 nm.
86. The method of claim 51 or 52, wherein the concentration of codeinone in the standard solution is in an amount of from about 1 ppm to about 500 ppm of solvent.
87. The method of claim 86, wherein the concentration of codeinone in the standard solution is in an amount of from about 1 ppm to about 20 ppm of solvent or 10 ppm of solvent.
88. The method of claim 87, wherein the concentration of oxycodone in the sample solution is about 50 mg/mL.
89. The method of claim 53 or 54, wherein the HPLC system comprises an autoinjector with an injection volume of from about 1 microliter to about 100 microliters.
90. The method of claim 95, wherein the injection volume is from about 1 microliter to about 10 microliters.
91. The method of claim 96, wherein the injection volume is about 5 microliters.
92. The method of claim 53 or 54, wherein the HPLC system utilizes isocratic elution.
93. The method of claim 53 or 54, wherein the HPLC system utilizes gradient elution.
94. The method of claim 73, wherein the mobile phase comprises from about 50% aqueous medium to about 85% aqueous medium.

95. The method of claim 73, wherein the mobile phase comprises from about 60% aqueous medium to about 75% aqueous medium.

96. The method of claim 73, wherein the mobile phase comprises from about 50% methanol to about 15% methanol.

97. The method of claim 73, wherein the mobile phase comprises from about 40% methanol to about 25% methanol.

98. The method of claim 73, wherein the mobile phase comprises about 50% aqueous medium and about 50% methanol.

99. The method of claim 73, wherein the mobile phase comprises about 60% aqueous medium and about 40% methanol; or about 75% aqueous medium and about 25% methanol.

100. The method of claims 51 or 52, wherein the oxycodone preparation is oxycodone hydrochloride active pharmaceutical ingredient.